The Impact of African American Race on Patterns of Care and Outcome in Prostate Cancer

Abstract

Objectives:

We evaluated whether African Americans (AA) with intermediate to high-risk prostate cancer receive similar treatment as white patients and whether any observed disparities are persistent with time, across age groups, or by insurance status.

Methods:

We used the Surveillance, Epidemiology, and End Results (SEER) database to identify 128,189 men with localized intermediate to high-risk prostate cancer (PSA $\geq$ 10 or Gleason $\geq$ 7 or T stage $\geq$ T2b) diagnosed from 2004 – 2010. We used multivariable logistic regression analyses to determine the impact of race on the receipt of definitive treatment and Fine-Gray competing risks regression to determine the impact of race on cancer mortality.

Results:

After adjusting for treatment, demographics, and prognostic factors, AA men had a higher risk of prostate-cancer specific mortality (AHR 1.12; 95% CI 1.01 – 1.25; $P = 0.03$). AA men were significantly less likely to receive curative-intent treatment than white men (Adjusted Odds Ratio [AOR] 0.82; 95% CI 0.79 – 0.86; $P < 0.001$). There was no evidence of this disparity narrowing over time ($P_{\text{interaction}}$ 2010 vs. 2004 = 0.490). Disparities in the receipt of treatment between AA and white men were significantly larger in high-risk (AOR 0.60; 95% CI 0.56 – 0.64; $P < 0.001$) than in intermediate-risk disease (AOR 0.92; 95% CI 0.88 – 0.97; $P = 0.04$), ($P_{\text{interaction}} < 0.001$). The adjusted odds of receiving definitive treatment for AA vs. white men

was 0.67 (95% CI 0.62 – 0.73; P <0.001) among men age <70, but was 0.60 (95% CI 0.55 – 0.66; *P* <0.001) among men age ≥70, suggesting increased racial disparity in the receipt of definitive treatment among older men ($P_{interaction}$ = 0.01). Among uninsured men, the adjusted OR for definitive treatment for AA vs. white was 0.38 (95% CI 0.27 – 0.54; P < 0.001), but among insured men, the adjusted OR was 0.62 (95% CI 0.57 – 0.66; P<0.001), ($P_{interaction}$ = 0.01).

Conclusions:

AA men with high-risk prostate cancer were significantly less likely to receive potentially life-saving definitive treatment when compared to white men. This disparity is worse in high-risk disease and among men age ≥70, and is not improving over time. Having health insurance was associated with a reduction in this racial treatment disparity, suggesting that expansion of health insurance coverage may help reduce racial disparities in the management of aggressive prostate cancer. Factors underlying these treatment disparities should be urgently studied, as they are potentially correctable contributors to excess prostate cancer mortality among AA patients.

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Glossary of Abbreviations

ACA- Affordable Care Act

AHR- Adjusted Hazard Ratio

AJCC

AOR- Adjusted Odds Ratio

CI- Confidence Interval

HR- Hazard Ratio

PCSM- Prostate Cancer Specific Mortality

PSA- Prostate Specific Antigen

NCCN- National Comprehensive Cancer Network

OR- Odds Ratio

SEER- Surveillance, Epidemiology, and End Results

Introduction

Prostate cancer represents the most commonly diagnosed non-cutaneous malignancy in men and there will be approximately 238,590 new cases of prostate cancer and 29,480 deaths due to prostate cancer in the United States in 2014; nearly 1 in 6 men will be diagnosed with prostate cancer in their lifetime.[1, 2] Risk stratification based on prostate-specific antigen (PSA), Gleason score, and clinical T-category predicts prostate cancer outcomes after treatment with curative intent for localized prostate cancer.[3-6] For patients with intermediate to high-risk prostate cancer, definitive treatments have been shown to decrease PCSM and improve overall survival and well defined guidelines have been established by the National Comprehensive Cancer Network (NCCN) based on these results.[3, 7-12]

African American men are more likely to be diagnosed with lethal forms of prostate cancer and are nearly twice as likely to die from prostate cancer when compared to white men.[1, 13] It is unknown how much of this is due to differences in biology versus disparities in treatment patterns and access to care.[14-17] Despite these differences in disease outcome and the well-defined NCCN guidelines mentioned above, racial and socioeconomic disparities in the management of prostate cancer have previously been suggested, although most prior studies have not been able to adequately describe and elucidate treatment patterns and survival outcome based on sociodemographic factors (including race) due to limited registry details and short follow-up available at the time of the studies.[14, 18, 19]

Prior large U.S. national cohort studies that examined racial disparities in prostate cancer used data from over a decade ago and were not able to assess racial differences in the management of prostate cancer by NCCN risk group given the lack of complete clinical information in the data sets used at the time of the studies.[14, 20] There is a paucity of

literature that examines racial disparities in prostate cancer by NCCN risk groups and evidence is conflicting as to whether racial disparities in the use of definitive treatment change with more advanced disease.[14, 21, 22]

Furthermore, most level 1-evidence for definitive therapy comes from studies focusing on men age < 65.[3, 4, 7, 8, 10-12, 23] Hence, the role of age in the management of patients with prostate cancer has been controversial.[24, 25] Many urologists postulate that the upper age limit for radical prostatectomy should be 70, and men over the age of 70 have been shown to receive curative treatment significantly less often than younger men.[24-29] Despite the challenges associated with managing older adults with prostate cancer, it has been suggested that definitive therapy results in significantly higher life expectancy as well as quality-adjusted life expectancy in men over the age of 70.[24, 26] Although efforts have been made to better understand cancer care patterns in older adults and by race, independently, there is little literature examining the relationship between age and racial disparities in the management of aggressive cancers. With a rapidly expanding population of minority older adults, it is critically important to understand this relationship.

Lastly, prior studies have not examined the relationship between race and insurance status. With the implementation of the Affordable Care Act (ACA) and ongoing expansion of health insurance coverage, it is critically important to understand the influence that health insurance may have on racial treatment patterns in cancer care.[30, 31]

In sum, prior studies that have examined prostate cancer outcome by race and other sociodemographics are either outdated and/or severely limited by the lack of details with regards to outcome by NCCN risk group and an updated effort with a contemporary cohort from a national database that more comprehensively captures treatment patterns and cancer outcome is

urgently needed to guide future interventions that seek to reduce racial disparities particularly among African American men in prostate cancer. Herein, we used the Surveillance, Epidemiology, and End Results (SEER) database to determine the contemporary impact of race on the of receipt of treatment with curative intent among patients with intermediate to high-risk prostate cancer and whether any disparities in management patterns changed with NCCN risk group and/or over time, across age groups, or by insurance status. Based on a growing body of literature which has demonstrated poorer healthcare outcome among minority and disadvantaged populations, we hypothesize that African American men with prostate cancer will receive worse care and suffer higher rates of cancer death when compared to non-minority white patients with prostate cancer. This study should guide future interventions which seek to reduce disparities in prostate cancer outcome.

Methods

Patient Population and Study Design

The Surveillance, Epidemiology and End Results Program (SEER) program, sponsored by the National Cancer Institute, collects and publishes cancer incidence, survival, and treatment data from population based cancer registries; the program captures approximately 97% of incident cancers and the 17 tumor registries encompasses about 26% of the US population.[32]

The SEER program was used to identify 128,189 (107,869 white; 20,320 African American) men with localized intermediate to high-risk prostate cancer, defined by prostate-specific antigen (PSA) $\geq$ 10 or Gleason score $\geq$7 or stage cT2b or higher,[3] diagnosed from 2004 – 2010, as previously described.[33] Gleason scores, as provided by the SEER program, represent the highest Gleason score identified at surgery (or at biopsy for non-surgically managed patients). Stage was determined using the AJCC 6th edition as provided by the SEER program.[32] The inclusion period was limited to 2004 – 2010, as 2004 represents the year that several of the covariates included in our multivariable analyses were introduced to SEER and 2010 represents the most recent year for which full information was available at the time of this study.

Initial management was defined as curative-intent treatment versus non-curative treatment. Curative-intent treatment was classified in accordance with the NCCN guidelines and included radical prostatectomy, external beam radiation therapy, brachytherapy, or any combination thereof.[3] SEER also provides information on patient refusal of recommended definitive surgery or radiation. Therefore, refusal of definitive treatment was classified as patient refusal of either surgery or radiation.

Race was classified as white and African American, as designated by the SEER program.[32] Income (computed as median household income) and educational status (computed as the percentage of residents ≥25 years of age with at least a high school education) were determined at the county level by linking to the 2000 United States Census; population means for each race were determined in order to provide the average county-level socioeconomic demographics for each race.[34] Residence type was also determined at the county level by linking to the 2003 United States Department of Agriculture rural-urban continuum codes.[35] We analyzed insurance coverage as a dichotomous variable given that SEER does not provide information on the specific type of insurance coverage that patients have. Specifically, a patient was considered "insured" if he was classified by SEER as "insured," "insured/no specifics," or "any Medicaid," and patients were considered "uninsured" if he was classified as such.

Statistical Analysis

The primary outcome of this study was the use of curative-intent treatment for intermediate to high-risk prostate cancer diagnosed from 2004 – 2010. Baseline clinical and demographic characteristics were compared using the t test and χ^2 test, as appropriate. Multivariable logistic regression analyses were used to determine the association between race and the use of curative-intent treatment using 3 models: model 1 was adjusted for age; model 2 was adjusted for age and prostate cancer-specific factors (cancer stage, Gleason score, and PSA); model 3 was adjusted for age, clinical factors, and other sociodemographics (marital status, income, education, and residence).[33] Men were only included (N = 116,084; White 84.0%, African American 16.0%) in analyses if they had data on the aforementioned covariates. These analyses were done for the entire cohort and also for men with intermediate-risk disease (PSA 10

– 20 or Gleason 7 or cT2b – T2c) and high-risk disease (PSA > 20 or Gleason 8 – 10 or cT3a – T4), separately. Multivariable sensitivity analyses including insurance status (only available from 2007 – 2010) and cause of other death (non-prostate mortality) within 5 years of follow-up as a proxy for comorbidity were repeated for men with high-risk disease. Also, multivariable logistic regression was used to determine whether there was an association between race and the rate at which curative-intent treatment was recommended but refused among men that did not undergo definitive therapy.

Next, management type (defined above under "Patient Population and Study Design") was analyzed stratified by race and age group (age < 70 vs age ≥ 70) among men with high risk prostate cancer, with χ^2 pairwise comparison tests made across each race and age group, as previously described.[36] After adjusting for sociodemographics (age group, race, residence [urban versus rural], marital status, income, education) and prostate cancer-specific prognostic factors (PSA, Gleason score, and stage), multivariable logistic regression was used to determine whether there was an interaction between age (age < 70 vs age ≥ 70) and race with respect to the use of definitive treatment among men with high risk prostate cancer with data on the aforementioned variables (N=58,874) via multiplicative multivariate logistic regression analysis. Furthermore, multivariable sensitivity analysis was done including other cause mortality (non-PCSM) within 5 years of follow-up as a proxy for comorbidity. After adjusting for the previously listed covariates in addition to receipt of definitive therapy, Fine and Gray's multivariable competing-risks regression was used to assess the secondary endpoints of the association of race on prostate cancer-specific mortality (PCSM) and also on other cause (non-PCSM) mortality (as a proxy for comorbidity).[37]

We then analyzed management type (defined above under "Patient Population and Study Design") stratified by race and insurance status among men with high risk prostate cancer, with χ^2 pairwise comparison tests made to compare across stratified groups, as previously described.[38] After adjusting for demographic factors (age, race, insurance status, marital status, residence [urban vs rural], income, education, Gleason score, and cancer stage), multivariable logistic regression was used to determine whether there was a statistical interaction between insurance status and race with respect to the use of definitive treatment. Since more than 1/3 of the uninsured patients were missing information on either PSA, Gleason score, or stage (a limitation inherent to SEER),[39] in order to not lose a disproportionately large proportion of uninsured patients from the multivariable analyses examining the influence of insurance status on disparities in prostate cancer outcome, we were only able to control for Gleason score and stage, since PSA was the most common missing variable among the uninsured (N = 64,277; including men with missing PSA values). Sensitivity logistic regression analyses were used to determine whether any observed interaction remained significant by insurance type (Medicaid vs uninsured and privately insured [no specifics] vs uninsured). Furthermore, Fine and Gray's multivariable competing-risks regression (adjusting for the aforementioned covariates in addition to receipt of definitive therapy) was used to assess the association of other cause (non-prostate cancer-specific) mortality as a proxy for comorbidity among uninsured men with at least 3 years of follow-up, given the lack of comorbidity information in SEER.[37]

Lastly, after adjusting for sociodemographics, prostate cancer prognostic factors, and initial management (receipt of curative-intent treatment vs not), Fine and Gray's multivariable competing-risks regression was used to assess the impact of race on prostate-cancer specific mortality (PCSM) as a secondary outcome measure.[37] Cumulative incidences of PCSM

stratified by race were generated from the competing-risks regression model and displayed graphically.[40] Point estimates and associated confidence intervals (CI) were generated and compared using Gray's k-mean P value. Furthermore, competing-risks regression was used to assess the impact of race on other cause (non-prostate cancer) mortality as a proxy for comorbidity.

All P values were two sided. The threshold of 0.05 was used to determine statistical significance. Statistical analyses were performed using R version 2.12.0 software (R Foundation for Statistical Computing, Vienna, Austria) for calculations relating to Gray's k-mean P value and STATA 13.1 (StataCorp, College Station, TX) for all remaining analyses. This study was approved by the institutional review board; a waiver for informed consent was obtained.

Results

Patient Characteristics

Baseline patient clinical and demographic characteristics are shown in Table 1.[33] Clinically small, but significant differences were noted for age, income, education, marital status, residence (urban vs rural), PSA, Gleason, stage, and NCCN risk category (intermediate vs high) when comparing African American and white patients. Notably, African American patients were more likely to be uninsured (3.8% vs 1.4%, $P < 0.001$), present with a PSA greater than 20ng/mL (24.6% vs 15.7%, $P < 0.001$) and high-risk disease (52.4% vs 48.7%, $P < 0.001$) and white men were more likely to present with cT3 – T4 disease (20.9% vs 16.3%, $P < 0.001$) when the two groups were compared.[33, 38]

Prostate-Cancer Specific Mortality

After a median follow-up of 39 months, cumulative incidence estimates of PCSM were significantly higher for African American men compared to white men among patients with intermediate to high-risk disease, with 5-year PCSM rates of 4.5% (95% CI 4.1 – 4.9%) for African American men and 3.4% (95% CI 3.3 – 3.6%) for white men ($P < 0.001$, Figure 1).[33] Furthermore, multivariable competing-risks regression analysis revealed an increased risk for PCSM among African American men compared to white men, with an Adjusted Hazard Ratio [AHR] of 1.12 (95% CI 1.01 – 1.25; $P = 0.03$), respectively.

Treatment Patterns

The raw unadjusted rates of initial management type stratified by race are provided for the entire cohort in Table 1. After adjusting for age, known prostate cancer prognostic factors , and sociodemographic factors on multivariable analysis, African American patients were significantly less likely to receive curative-intent treatment (Table 2) when compared to white men among patients with intermediate to high-risk prostate cancer (Adjusted Odds Ratio [AOR] 0.82; 95% CI 0.79 – 0.86; $P < 0.001$).[33] There was a significant interaction between race and risk group ($P_{interaction} < 0.001$) such that racial disparities in the receipt of treatment between African American and white men were significantly higher in high-risk disease (Adjusted OR 0.60; 95% CI 0.56 – 0.64; $P < 0.001$) than intermediate-risk disease (Adjusted OR 0.92; 95% CI 0.88 – 0.97; $P = 0.04$).

When analyzed on a year-by-year basis from 2004 – 2010, African American men were consistently less likely to receive curative treatment when compared to white men among patients with high-risk disease ($P < 0.001$ for each year, from 2004 – 2010). As displayed graphically in Figure 2, these disparities did not appear to improve over time ($P_{interaction}$ 2010 vs. 2004 = 0.490).[33]

Of note, among men with high-risk disease who did not receive definitive therapy, there was no difference in the adjusted odds of refusing recommended curative-intent treatment between African American and white patients on multivariable analysis (Adjusted OR 1.04; 95% CI 0.93 – 1.17; $P = 0.45$).

Treatment Patterns Stratified by Race and Age Group

Unadjusted absolute management rates stratified by race (African American vs white) and age group (age < 70 vs age ≥ 70) as analyzed by univariable analysis are displayed in Table 3.[36] Of note, African American men age 70 and above had the lowest rate of definitive therapy (52.0%) among men with high-risk prostate cancer. AA men under the age of 70 were more likely to receive definitive therapy when compared to African American men age 70 and over (81.7% vs 52.0%; $P < 0.001$). Similarly, white men age 70 and above were less likely to receive definitive therapy when compared to white men under the age of 70 (64.8% vs 91.1%; $P < 0.001$), however the absolute rate difference was not as pronounced as among the African American men detailed above. Furthermore, among men age 70 and over, African American men were significantly less likely to receive definitive treatment when compared to white men (52.0% vs 64.8%; $P < 0.001$).

There was a significant interaction between age group (age < 70 vs age ≥ 70) and race ($P_{interaction} = 0.01$) such that the adjusted odds of receiving definitive treatment for African American vs. white was 0.67 (95% CI 0.62 – 0.73; P < 0.001) among men younger than 70, but among men age 70 and older, the adjusted odds was 0.60 (95% CI 0.55 – 0.66; $P < 0.001$), suggesting an increased racial gap in the delivery of definitive treatment between African American and white patients among men age 70 and older (Table 4).[36] Furthermore, in a sensitivity analysis we found that even after adjusting for non-PCSM mortality within 5 years (as a proxy for baseline comorbidity), the interaction between race and age remained significant ($P_{interaction} = 0.01$) and the disparity in the receipt of definitive treatment remained higher among men age ≥ 70 (AOR 0.61 among men 70 and older vs 0.68 among men age < 70; Table 5).[36]

Association of Race on PCSM and Other Cause Mortality among Men Age > 70

After a median follow-up of 35 months, cumulative incidence estimates of PCSM were significantly higher among African American men age ≥ 70 with high-risk disease when compared to white men, with 5-year PCSM rates of 15.8 % (95% CI 14.5 – 17.2%) and 12.5% (95% CI 12.2 – 13.2%), respectively (P < 0.001). Furthermore, African American men age ≥ 70 with high-risk prostate cancer had a higher risk of PCSM compared to white men on multivariable analysis (AHR 1.20; 95% CI 1.02 – 1.38; $P = 0.02$). However, there was no difference in other cause (non-PCSM) mortality between African American and white patients age ≥ 70 (AHR 0.99; 95% CI 0.92 – 1.08; $P = 0.91$), suggesting no underlying difference in comorbidity that might have explained some of the disparity in the receipt of definitive therapy.

Treatment Patterns Stratified by Race and Insurance

Treatment patterns stratified by race and insurance status among men with high-risk prostate cancer are shown in Table 6.[38] Uninsured African American men had the highest rate (27.8%) of not receiving definitive treatment among men with high-risk prostate cancer. Insured African American men were more likely to undergo definitive therapy (84.5% vs 72.2%; $P < 0.001$) when compared to uninsured African American men. Similarly, white insured men were more likely to receive definitive therapy when compared to uninsured white men, although the difference (89.4% vs 84.3%, $P < 0.001$) was not as pronounced as for African American men with and without insurance, as detailed above.

On logistic regression analysis, insured men with high risk prostate cancer were significantly more likely to receive definitive treatment when compared to uninsured men on

both univariable (OR 1.91; 95% CI 1.65 – 2.22; P < 0.001) and multivariable analysis (AOR 1.79; 95% CI 1.50 – 2.14; $P < 0.001$). A significant interaction between race and insurance status was found ($P_{interaction} = 0.01$) such that insurance coverage was associated with a reduction in racial disparity between African American and white patients with regards to receipt of definitive therapy. The unadjusted OR for definitive treatment for African American vs. white was 0.49 (95% 0.36 – 0.65; P < 0.001) among uninsured men, while the OR was 0.65 (95% CI 0.61 – 0.69; P < 0.001) among insured men. Furthermore, after adjustment for sociodemographics and cancer-specific factors, the AOR for definitive treatment for African American vs. white was 0.38 (95% CI 0.27 – 0.54; P < 0.001) among uninsured men, while the AOR was 0.62 (95% CI 0.57 – 0.66; P<0.001) among insured men. This significant interaction also suggests that the effect of insurance status on the receipt of definitive treatment differed by race. Specifically, African American men appeared to have a larger increase in the receipt of definitive therapy when comparing uninsured to insured men (AOR 2.23; 95% CI 1.72 – 2.88; P <0.001) than white men did (AOR 1.47; 95% CI 1.15 – 1.89; $P = 0.002$; [Table 7]).[38] Furthermore, relative to white-insured men, African American men with insurance had more than twice the odds of receiving definitive treatment when compared to uninsured- African American men (Figure 3).

Sensitivity analyses revealed that when stratifying results by insurance type (privately insured [no specifics] vs any Medicaid) that significant interactions remained between race and insurance status. Specifically, there were significant interactions between race and private insurance/no specifics ($P = 0.007$) and also between race and Medicaid ($P = 0.04$) such that disparities in receipt of treatment were reduced from an AOR for definitive treatment for African American vs white men of 0.38 (95% CI 0.27 – 0.54; $P < 0.001$) among uninsured men to 0.65

(95% CI 0.60 – 0.70; $P < 0.001$) among privately insured men and to 0.58 (95% CI 0.46 – 0.73; $P < 0.001$) among men with Medicaid (Table 8).[38]

Association of Race on Other Cause Mortality among Uninsured Men

As a sensitivity analysis, we found that the risk of other cause (non-prostate cancer-specific) mortality (analyzed as a proxy for comorbidity) among uninsured men with at least 3 years of follow-up was not different between white and African American men ($P = 0.54$). This suggests that there is little difference in comorbidity status among the uninsured and a low likelihood that the increased disparity in receipt of definitive therapy among the uninsured was due to comorbidity differences.

Discussion

In this study we found that, after adjusting for sociodemographics, known prostate cancer prognostic factors, and receipt of definitive treatment, African American men with intermediate to high-risk prostate cancer are at a 12% increased relative risk for PCSM when compared to white men; however, African American men receive curative-intent treatment 18% less often relative to white men. This disparity is even greater among high-risk patients, as African American men with high-risk disease were 40% less likely to receive curative treatment compared to white patients. The magnitude of this disparity did not change over time. Furthermore, African American men with high-risk prostate have a 20% increased risk of PCSM when compared to white men among patients age $\geq$ 70. Despite this excess mortality, our results revealed greater disparities in the receipt of definitive therapy among men 70 and older. Specifically, we found that African American men with high-risk prostate cancer under the age of 70 were 33% less likely to receive definitive therapy when compared to white men from the same age group, while African American men age $\geq$ 70 were 40% less likely to receive definitive therapy relative to white men age $\geq$ 70. Lastly, our results demonstrated that there was a significant interaction between race and insurance status on multivariable logistic regression analysis such that uninsured African American men were 62% relatively less likely to receive definitive treatment when compared to white uninsured men, while insured African American men were only 38% relatively less likely to receive definitive treatment when compared to insured white men. Similarly, when examining the relationship between insurance status and race on the receipt of definitive treatment, the significant interaction suggested that African American men derived a larger benefit from being insured versus uninsured with respect to receipt of definitive therapy than white men did.

This study is novel and important because it identifies what are potentially immediately actionable contributors to excess prostate cancer mortality in African American men. Our study in a large national contemporary cohort comprehensively reports on racial treatment disparities as a highly problematic issue that has been persistent with time, that is alarmingly worse among men with high-risk disease who need treatment most, that is worse among older men, and that is improved by being insured and having greater access to care. Furthermore, our study reports on worse prostate cancer-specific mortality among African American men that persists when controlling for potentially confounding sociodemographic variables. The underlying reasons for these racial disparities must be carefully studied and these findings could guide policy level intervention, as they identify potentially correctable contributors to excess prostate cancer mortality among African American patients.

Our findings have important implications for racial treatment patterns in a new era defined by healthcare coverage expansion and the implementation of the Affordable Care Act.[1, 31] Our results suggest that insurance coverage may help reduce racial disparities in treatment patterns for aggressive cancers, likely by increasing access to care. Based on these results, it could be postulated that with the expansion of health care coverage, one might expect greater access to care and a reduction in racial disparities in cancer-care patterns. This would be particularly beneficial for African American men with high-risk prostate cancer who die from their cancer more frequently than white men and who experience a longer time to diagnosis and are less likely to receive definitive treatment even among patients with similar disease characteristics.[1, 20, 41] Of note, addressing socioeconomic and racial disparities was one of the major aims of the ACA.[30, 31] Nevertheless, it may be premature to directly link the results of this study to the ACA.

There is a paucity of literature examining the interaction between race and insurance and its association with cancer care patterns. Previous studies focusing on insurance status in healthcare have indicated that being insured is associated with increased access to care and decreased morbidity and mortality in the management of patients (including those undergoing radical prostatectomy).[42-45] Furthermore, it has been suggested that African American men and uninsured patients are less likely to have access to high-volume urologic surgeons and hospitals with access to robotic surgery.[46] However, there is literature to suggest that neither African American race nor insurance status are associated with the odds of receiving guideline-concordant care.[21] As pointed out by the authors of the study, the results were based on a small cohort (N = 777) of patients from North Carolina that may not be generalizable to the broader U.S. population and the analyses examining insurance status lacked precision due to the small number of uninsured patients (N=63).[21] Nevertheless, this study by Ellis and colleagues represents a paradigm shift in the method by which disparities in prostate cancer should be studied and certainly guided the methods and design of this study; namely, disparities should be studied within, not across, NCCN risk groups. Still, studies have not specifically examined the interaction between race and insurance status and it is difficult to determine how insurance coverage might influence racial disparities in cancer care patterns based on prior literature.

Furthermore, our findings also have important implications for racial cancer care patterns in an aging population that is becoming more racially and ethnically diverse and that will continue to be impacted by a greater burden of prostate cancer among older adults. [1, 24, 47] Among men ages 60 – 79, the leading cause of death in the United States is cancer, with prostate cancer being the second leading cause of cancer death.[1] The number of men age 65 and above in America increased by over 20 million from 2000 to 2010 and is expected to increase by

another 25 million over the next decade, with the population of older adults from minority groups expected to grow by nearly 25%.[47] Given an increasing population of older adults (especially from minority groups) and increasing life expectancy in the United States, one can expect a greater number of older minority men to be diagnosed with prostate cancer in the near future.[1, 47] Furthermore, with the new U.S. Preventive Services Task Force (USPSTF) recommendations against prostate-specific antigen (PSA) screening, there will likely be migration toward higher stage and grade among men with newly diagnosed prostate cancer.[48, 49] Based on our results, it can be postulated that without immediate intervention, one could expect an increase in racial disparities in the delivery of definitive treatment for high-risk prostate cancer in an aging population. This would be particularly detrimental to African American men with aggressive prostate cancer who die from their cancer at higher rates than any other population and for whom potentially curative treatment is particularly important.

The causes of excess prostate-cancer mortality among African American men are likely multifactorial. African American men may have a biologic predisposition for aggressive disease, have poorer access to care, experience treatment delays, and/or receive care from lower volume and quality centers, all of which could lead to worse survival after a median follow-up of only 39 months. Unfortunately, SEER does not provide information on these potential factors of excess mortality and so we were unable to determine their impact on mortality. Although it is difficult to determine the underlying reasons for increased racial disparities in the treatment of men with prostate cancer, most of the literature has focused on patient preference, mistrust, socioeconomic status, provider and system level factors, and comorbidities as potential drivers of disparity. [14, 18, 19, 22, 41, 50-54]

To address some of these previously postulated hypotheses of drivers of prostate cancer disparities, we completed several sensitivity analyses. First, although there is some evidence from the lung cancer literature that African American adults are more likely to refuse recommended treatment,[55] there was no difference in the rate at which treatment recommended by a provider was refused by African American vs. white patients with high-risk disease (OR 1.04; P = 0.45). Nevertheless, mistrust by African American patients has been observed previously among men with prostate cancer,[51] and it is difficult to rule out the possibility that subtle mistrust of the healthcare system led to less definitive treatment. Second, although lack of insurance can be a barrier to receiving adequate care, and insurance was a significant driver of treatment in our study, we found that racial disparities in the receipt of definitive treatment remained significant even after adjusting for insurance status (Table 2). Third, it is conceivable that African American men had higher baseline comorbidity and so the disparity in treatment may not have been entirely inappropriate, but we found that even after adjusting for non-prostate mortality within 5 years of follow-up (as a proxy for comorbidity), the disparities remained significant (Table 2). Provider level factors may also contribute to the observed race-risk interaction and disparity. For example, if providers over-estimate the comorbidity burden of African American patients, this may lead them to recommend definitive treatment less frequently. Alternatively, providers may not be sufficiently communicating to African American men with higher risk disease that their disease is significantly more lethal and needs to be treated more urgently than if they had intermediate-risk disease. This possibility is suggested by the fact that among white patients, the treatment rate increases by 14.1% as patients move from intermediate to high risk disease, but among African American patients, the treatment rate increases by only 7.3% between intermediate and high risk disease. Lastly, it has been

shown that physicians tend to underestimate the life expectancy of patients with high-risk prostate cancer,[52] and it could be the case that this underestimation is larger among African American men leading to more disparate patterns of care among older men, although there is no variable to test that assumption in SEER.

We also completed sensitivity analyses to further examine some of the aforementioned hypotheses for underlying reasons for increased disparities in the treatment of older adults with prostate cancer. First, it is possible that African American men may have had higher comorbidity than white men among patients 70 and older and the excess disparity in receipt of treatment among men age $\geq$ 70 may not have been entirely inappropriate. However, we found that among men age $\geq$ 70 with high-risk prostate cancer, African American men had no difference in the risk of other cause mortality when compared to white men on multivariable analyses (Adjusted HR 0.99; $P = 0.91$) . Furthermore, we found that even after adjusting for non-PCSM within 5 years (as a proxy for baseline comorbidity), although the comorbidity proxy was a significant driver against the receipt of definitive therapy, the interaction between race and age remained significant ($P_{\text{interaction}} = 0.01$) and the disparity in the receipt of definitive treatment remained higher among men age $\geq$ 70 (Table 4).

To put our study into historical context, Underwood et al found in a SEER cohort from 1992 – 1999, that African American men with moderately differentiated prostate cancer (Gleason 5 – 7) and poorly/undifferentiated prostate cancer (Gleason 8 – 10) were 46% and 51% less likely to undergo definitive treatment when compared to white patients, respectively,[14] and other more recent studies have also noted racial disparities in the use of potentially curative treatment among men with prostate cancer.[21, 22, 56] However, results have been conflicting as to the impact of risk-group on racial disparities. For example, although these disparities in

management appear in some studies to be larger among men who might benefit more from treatment,[22, 56] Ellis and colleagues did not find differences in racial disparities by NCCN risk groups when looking at a North Carolina state database.[21] Our study is unique in that it elucidates disparities in cancer-specific outcomes and patterns of oncologic care for prostate cancer across NCCN risk groups, and across age groups and insurance status in a large national population. In light of these results, efforts should be made to ensure that all men with aggressive disease receive curative treatment at similar rates regardless of sociodemographics. Addressing the underlying barriers to receipt of treatment could potentially improve outcomes for African American men.[21, 57, 58] Although there is little evidence of interventions that reduce disparities in patterns of cancer care and outcomes, the Centers for Disease Control and Prevention (CDC) has partnered with public health agencies, providers, and communities to facilitate a national effort aimed at reducing disparities in cancer.

Although more research is needed to further elucidate the underlying reasons for disparities in cancer-outcomes, particularly for African American men with prostate cancer, our results demonstrate an actionable item that can be implemented in the imminent future to reduce these disparities. Specifically, expanding health care insurance (including Medicaid) may lead to more equal treatment patterns across races for aggressive cancers. Additionally, shared decision making as encouraged by the Affordable Care Act could also lead to more accurate risk perceptions and a greater likelihood of receiving care aligned with patient values.[30, 58] These could be some of the major benefits of expansion of health care through the Affordable Care Act.[30] Notably, a similar reduction in racial disparities in treatment patterns for receipt of minimally invasive surgery (laparoscopic cholecystectomy and appendectomies) was observed

after the 2006 Massachusetts insurance expansion by Loehrer et al, however this study did not examine patterns of cancer-care.[45]

Nevertheless, even among insured men, our results display that disparities in the receipt of definitive treatment for high-risk cancer still exist and closing the gap in disparate treatment patterns will likely not be done by expanding insurance coverage alone. Well-defined treatment options for high-risk prostate cancer are likely being underused for African American men even when adjusting for health insurance coverage, as demonstrated by the results in our study. Specifically, efforts in health care should be made to treat African American men with high-risk cancers in a culturally competent manner at similar rates as white men, across insurance status and other socioeconomic determinants.

Ideally, the goal of reducing disparities in the receipt of potentially curative treatment is to achieve equally high rates of treatment when it is warranted among all groups of patients, which will in turn close racial disparities. Specifically, following the well-delineated NCCN guidelines (which ubiquitously recommend definitive therapy for men with high-risk disease, without specifying age or life expectancy cutoffs for observation) in a culturally competent and compassionate manner is critically important to closing disparity gaps. To reduce disparate outcomes in aggressive cancers it is clear that there will need to be equal access to cancer screening, interventions at the community level to educate populations about the risks of aggressive cancers, clinical trials which include adequate numbers of minority participants, and prospective research of interventions that can help determine the most efficacious approach to alleviating cancer disparities.[55, 57, 59, 60] These interventions will take time before targets are achieved. Meanwhile, one method of achieving more immediate reductions in disparities in cancer outcomes may be done by setting race-neutral treatment of aggressive disease as a quality

metric that an institution must achieve to reach a certain quality status. Although there are no national benchmarks for prostate cancer care, an 80% benchmark for adherence to guideline-concordant care has been proposed by Ellis and Colleagues.[21] Several payers are now expecting providers to adhere to treatment pathways, and there has been a gradual introduction of pathway databases where the type of treatment received by each patient can be tracked on a provider level to determine how often the provider deviated from the standard pathway. Ultimately, by measuring adherence to pathways for high-risk prostate cancer, we may begin to see these racial disparities narrow. Similarly, given that it has been suggested that African American men have less access to high quality care and high volume centers, an effort should be made to ensure that African American men have equal access to affordable high volume and quality health centers.[46]

There are several potential limitations to our study. The SEER database does not have information on comorbidity, and so it is conceivable that the decreased rate of treatment among African American patients is not entirely inappropriate. We completed a sensitivity analysis and found that African American men had a higher risk of other-cause mortality (AHR 1.33; 95% CI 1.23 – 1.43; P < 0.001**)**, suggesting that they may have higher baseline comorbidity in this cohort. However, as mentioned above, when we adjusted for insurance status and other-cause mortality as a proxy for comorbidity in the logistic regression model for receipt of curative-intent treatment, the odds ratio for treatment among African American men only increased from 0.60 to 0.63 ($P < 0.001$) (Table 2), suggesting any comorbidity likely accounts for only a small component of the disparity in treatment. We also found that the risk of other cause (non-prostate cancer-specific) mortality (analyzed as a proxy for comorbidity) among uninsured men with at least 3 years of follow-up was not different between white and African American men ($P =$

0.54), suggesting little difference in comorbidity status among the uninsured. Additionally we found that the risk of other cause of death (non-PCSM) was not different (HR 0.99; $P = 0.91$) between white and African American men age ≥ 70, suggesting little to no difference in comorbidities between the two groups. Furthermore, when adjusting for non-PCSM mortality (as a proxy for comorbidity) via multivariable sensitivity analysis, the race-age interaction remained significant with greater disparities in treatment among men 70 and older (Table 5). Although this comorbidity proxy is based on the best information we have to approximate comorbidity information in SEER, it likely still does not completely capture comorbidity status and so it still cannot be ruled out that African American, uninsured, or older men suffered from higher rates of comorbidity in our cohort. Second, our statistical adjustments for income, education, and residence (urban vs rural) were linked at the county, not individual, level as provided by the state and county codes in SEER. Third, in regards to secondary endpoints, the median follow-up of this study was only 39 months; nevertheless, significant differences in PCSM were already observed between white and African American men. Longer follow-up is required to determine whether the magnitude of the observed differences in PCSM will increase with time. Fourth, we were not able examine whether racial disparities in health care prior to diagnosis of prostate cancer, such as access to prostate cancer screening, may have impacted survival. Previous studies have shown lower rates of undergoing proper screening and staging among African American men.[53] Fifth, SEER replaces the biopsy Gleason score with the prostatectomy Gleason score for surgically managed patients, thus these results may have been underestimates of the true magnitude of the difference in PCSM between African American and white men given that African American men are more likely to get upgraded at prostatectomy;[17] thus, for example, the patient with Gleason 6 at biopsy but Gleason 7 at

radical prostatectomy patient (who is more likely to have better outcomes) is more likely to be African American than white. Nevertheless, our findings still revealed that African American men have worse PCSM outcomes when compared to white patients. Sixth, SEER does not provide information on quality metrics (including androgen deprivation therapy, provider volume, and complications) of the centers at which patients are receiving care or time from diagnosis to receipt of treatment. Therefore, as has previously been shown, African American men may be receiving their care at lower volume centers with poorer quality metrics and may be experiencing delays in receipt of treatment which may be contributing to some of the excess PCSM observed in our study.[41] Seventh, it is possible that SEER does not capture all episodes of curative treatment. Specifically, it is possible that African American men may have experienced more delays from diagnosis to treatment, and some curative therapies therefore may not have been captured by the registries. Future SEER studies should aim to determine the extent to which this limitation exists. Eighth, SEER does not provide information about insurance coverage periods or the details of the insurance plans that patients have and so we analyzed insurance coverage as a binary variable. Nevertheless, on sensitivity analyses, the associations and interactions observed in this study remained when stratifying by insurance type as broadly provided by SEER (Medicaid vs uninsured or private insurance [no specifics] vs uninsured; Table 8). Ninth, there was a small number of uninsured patients in our cohort (N = 1,136). Although this study is limited by the number of uninsured patients that are included, previous studies focusing on the impact of both race and insurance status on the receipt of definitive therapy for prostate cancer had fewer than 65 uninsured patients.[21] Tenth, over 35% of the uninsured patients were missing information on either PSA, Gleason score, or stage; although this is a limitation inherent to SEER, in order to not lose a large proportion of uninsured patients

from our multivariable analyses, we were only able to control for Gleason score and stage, since PSA was the most common missing variable among the uninsured.

Conclusion, Summary, and Future Direction

Despite the potential limitations of our SEER-study, our findings in a large national contemporary cohort indicate that African American men with intermediate to high-risk prostate cancer are at higher risk for PCSM and undertreatment when compared to white patients independent of known prostate cancer prognostic factors and sociodemographic factors. This disparity in receipt of definitive treatment is significantly greater among men with high-risk disease and among men age ≥70, and is not improving over time. Having health insurance was associated with a reduction in this racial treatment disparity. This study is important in that it highlights previously understudied and undervalued significant relationships between race and NCCN risk group, race and age, and also between race and insurance status. With the ongoing expansion of healthcare and an aging population and a greater burden of prostate cancer in older minority adults on the horizon, these results both suggest that expansion of health insurance coverage may help reduce racial disparities in the management of aggressive prostate cancer and highlight the need for urgent intervention that should be made to ensure that potentially curative treatment is delivered to all patients regardless of race, age or background when warranted in order to prevent increasing disparities in cancer care.

Prior Publishing Statement

Several portions of the Abstract, Introduction, Methods, Results, Discussion, and Conclusion were adapted from previously published work. [33, 36, 38]

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Table 1. Baseline clinical and demographic characteristics. *Previously published. [33]*

Characteristic		**White** (N = 97,548)	**African American** (N = 18,536)	***P*-value (AA vs White)**
Age, years, mean (SD)		66.4 (8.9)	63.6 (9.0)	< 0.001
Income, USD, mean (SD) [a]		47,000 (12,000)	44,000 (11,000)	< 0.001
Percent that completed high school, mean (SD) [a]		80.1 (7.6)	78.0 (7.0)	<0.001
Residence, (%)†				<0.001
	Rural	12.8	9.2	
	Urban	87.2	90.8	
Married, (%)				<0.001
	No	21.9	40.0	
	Yes	78.1	60.0	
Insured, (%)				<0.001
	No	1.3	3.8	
	Yes	98.7	96.2	
PSA, median (IQR)		6.3 (4.7 – 9.7)	7.1 (4.9 – 19.2)	<0.001
PSA				<0.001
	< 10 ng/ml	75.9	66.4	
	10 – 20 ng/ml	8.4	9.0	
	> 20 ng/ml	15.7	24.6	
Gleason				0.04
	Gleason $\leq$ 7	74.3	73.5	
	Gleason 8 – 10	25.7	26.5	
Stage, (%)				<0.001
	$\leq$ T2c	79.1	83.7	
	T3a – T4	20.9	16.3	
NCCN Risk Category				<0.001
	Intermediate	51.3	47.6	
	High	48.7	52.4	
Treatment Received				<0.001
	Not Managed Curatively	26.0	30.0	
	Radical Prostatectomy	25.5	19.3	

	Radiation (EBRT and/or Brachytherapy)	45.1	48.1	
	Combination Therapy	3.4	2.6	

[a] County-level data

Abbreviations: AA = African American; EBRT = External Beam Radiation Therapy; N = Number; NCCN = National Comprehensive Cancer Network; SD = Standard Deviation; USD = United States Dollar

Table 2. Multivariable logistic regression analyses for odds of receiving curative-intent treatment (radical prostatectomy, external beam radiation therapy, brachytherapy, or any combination thereof) for men diagnosed with prostate cancer from 2004 – 2010, according to National Comprehensive Cancer Network risk stratification. (N = 116,084: White 84.0%, AA 16%). ($P_{interaction}$ intermediate-risk vs. high-risk disease < 0.001). *Previously published. [33]*

Characteristic		**Multivariable Analysis**	
		Adjusted OR for receipt of curative-intent treatment (95% CI)	*P*-value
Intermediate to High-Risk Prostate Cancer (Entire Cohort, N = 116,084)			
Race (Model 1) [a]			< 0.001
	White	1.0 (Ref)	
	African American	0.67 (0.65 – 0.70)	
Race (Model 2) [b]			< 0.001
	White	1.0 (Ref)	
	African American	0.76 (0.74 – 0.79)	
Race (Model 3) [c]			< 0.001
	White	1.0 (Ref)	
	African American	0.82 (0.79 – 0.86)	
Intermediate-Risk Prostate Cancer (N = 58,874)			
Race (Model 1) [a]			< 0.001
	White	1.0 (Ref)	
	African American	0.86 (0.82 – 0.90)	
Race (Model 2) [b]			< 0.001
	White	1.0 (Ref)	
	African American	0.88 (0.84 – 0.92)	
Race (Model 3) [c]			0.04
	White	1.0 (Ref)	

	African American	0.92 (0.88 – 0.97)	
High-Risk Prostate Cancer (N = 57,210)			
Race (Model 1) [a]			<0.001
	White	1.0 (Ref)	
	African American	0.40 (0.38 – 0.43)	
Race (Model 2) [b]			<0.001
	White	1.0 (Ref)	
	African American	0.54 (0.51 – 0.57)	
Race (Model 3) [c]			<0.001
	White	1.0 (Ref)	
	African American	0.60 (0.56 – 0.64)	
Sensitivity Analysis for men with High-Risk Prostate Cancer (N = 32,662) [d]			
Race			<0.001
	White	1.0 (Ref)	
	African American	0.63 (0.58 – 0.69)	
Insurance Status			< 0.001
	Insured	1.0 (Ref)	
	Uninsured	0.39 (0.32 – 0.48)	
Comorbidity / Death due to other cause			< 0.001
	No death due to other cause / No Comorbidity	1.0 (Ref)	
	Death due to other cause / Comorbidity	0.34 (0.29 – 0.40)	

[a] Adjusted for age.

[b] Adjusted for age and cancer-specific factors (cancer stage, Gleason score, and PSA).

[c] Adjusted for age, cancer-specific factors (cancer stage, Gleason score, PSA), and sociodemographic factors (marital status, income, education, residence).

[d] Adjusted for age, cancer-specific factors (cancer stage, Gleason score, PSA), and sociodemographic factors (marital status, income, education, residence), insurance status, and death due to other cause within 5 years of follow-up (as a proxy for comorbidity).

Abbreviations: OR = Odds Ratio

Table 3. Proportion of men diagnosed with high-risk prostate cancer from 2004 – 2010 (N=58,874) receiving definitive therapy stratified by race (African American vs white) and age group (age ≥ 70 vs age < 70). *Previously published. [36]*

Therapy	**%White Age ≥ 70** (N =19,153)	**%White Age < 70** (N =29,722)	**%African American Age ≥ 70** (N = 2,865)	**%African American Age < 70** (N = 7,134)	***P*-value**[a]
Definitive Therapy	64.8	91.1	52.0	81.7	$P < 0.001$
No Definitive Therapy	35.2	8.9	48.0	18.3	$P < 0.001$

[a] $P < 0.001$ with all pairwise comparisons across each row

Table 4. Assessment of effect modification between age group (age ≥ 70 vs age < 70) and race (AA vs white) for the outcome of receipt of definitive therapy. All men were diagnosed with high-risk prostate cancer from 2004 – 2010 (N=58,874). *Previously published. [36]*

Characteristic			**Multivariable Analysis**[b]	
			Adjusted OR (95% CI)[a]	*P*-value
Interaction for receipt of definitive therapy				0.01[c]
Age Group				
Age < 70				
	Race			< 0.001
		White	1.0 (ref)	
		AA	0.67 (0.62 – 0.73)	
Age ≥ 70				
	Race			< 0.001
		White	1.0 (ref)	
		AA	0.60 (0.55 – 0.66)	

[a] Adjusted OR comparing the rate of receipt of definitive treatment.

[b] Multivariable analyses are adjusted for age group, income, education, residence, marital status, prostate-specific antigen (PSA), Gleason score, and cancer stage.

[c] P value for interaction term tests whether there is a significant difference in the OR between white and African American patients.

Abbreviations: AA = African American; OR = Odds Ratio

Table 5. Sensitivity analysis of interaction and effect modification between age group and race for the outcome of receipt of definitive therapy, including non-prostate mortality as a proxy for comorbidity. All men were diagnosed with high-risk prostate cancer from 2004 – 2010 (N=58,874). *Previously published. [36]*

Characteristic			**Multivariable Analysis**[b]	
			Adjusted OR (95% CI)[a]	*P*-value
Interaction for receipt of definitive therapy				0.01[c]
Age Group				
Age < 70				
	Race			< 0.001
		White	1.0 (ref)	
		AA	0.68 (0.63 – 0.74)	
	Comorbidity / Non-Prostate Mortality			< 0.001
		No Comorbidity / Non-Prostate Mortality	1.0 (ref)	
		Comorbidity / Non-Prostate Mortality	0.38 (0.32 – 0.45)	
Age ≥ 70				
	Race			< 0.001
		White	1.0 (ref)	
		AA	0.61 (0.56 – 0.67)	
	Comorbidity / Non-Prostate Mortality			< 0.001
		No Comorbidity / Non-Prostate Mortality	1.0 (ref)	
		Comorbidity / Non-Prostate Mortality	0.44 (0.40 – 0.49)	

[a] Adjusted OR comparing the rate of receipt of definitive treatment.

[b] Multivariable analysis is adjusted for age, income, education, residence, marital status, prostate-specific antigen (PSA), Gleason score, and cancer stage.

[c] P value for interaction term tests whether there is a significant difference in the OR between white and African American patients.

Abbreviations: AA = African American; OR = Odds Ratio

Table 6. Proportion of men diagnosed with high-risk prostate cancer receiving each therapy type stratified by race and insurance status (N = 64,277; including men with missing PSA values). *Previously published. [38]*

Therapy	**%White Insured** (N = 53,338)	**%White Uninsured** (N = 753)	**%African-American Insured** (N = 9,803)	**%African-American Uninsured** (N = 383)	[a]***P*-value**
Non-Definitive Therapy	10.6	15.7	15.5	27.8	<0.001
Definitive Therapy	89.4	84.3	84.5	72.2	<0.001

[a] P < 0.001 with all pairwise comparisons across each row

Table 7. Assessment of effect modification between insurance status and race for the outcome of employment of definitive therapy. All men were diagnosed with high-risk prostate cancer (N = 64,277; including men with missing PSA values). *Previously published. [38]*

Characteristic		[a]**Multivariable Analysis**	
		Adjusted OR (95% CI)	*P*-value
Interaction for employment of definitive therapy[b]			0.01[b]
White Men			
	Uninsured	Ref (1.0)	0.002
	Insured	1.47 (1.15 – 1.89)	
African-American Men			
	Uninsured	Ref (1.0)	< 0.001
	Insured	2.23 (1.72 – 2.88)	

[a] Multivariable analyses are adjusted for age, income, education, residence, cancer stage, and Gleason score.

[b] P value for interaction term tests whether there is a significant difference in the OR between white and African-American patients.

Abbreviations: OR = Odds Ratio

Table 8. Sensitivity analysis of effect modification between insurance status (by type: privately insured/no specifics vs uninsured and Medicaid vs uninsured) and race for the outcome of employment of definitive therapy. All men were diagnosed with high-risk prostate cancer (N = 64,277; including men with missing PSA values). *Previously published. [38]*

Characteristic		[a]**Multivariable Analysis**	
		Adjusted OR (95% CI)	*P*-value
Uninsured Patients			
Race			
	White	Ref (1.0)	< 0.001
	African American	0.38 (0.27 – 0.54)	
Privately Insured (No Specifics) Patients			
Interaction for employment of definitive therapy[b]			0.007[b]
Race			
	White	Ref (1.0)	< 0.001
	African American	0.65 (0.60 – 0.70)	
Medicaid Patients			
Interaction for employment of definitive therapy[c]			0.04[c]
Race			
	White	Ref (1.0)	< 0.001
	African American	0.58 (0.46 – 0.73)	

[a] Multivariable analyses are adjusted for age, income, education, residence, cancer stage, and Gleason score.

[b,c] Value for interaction term tests whether there is a significant difference in the OR between uninsured and privately insured (no specifics) patients [[b]] or between uninsured and Medicaid patients [[c]].

Abbreviations: OR = Odds Ratio

Figure 1. Cumulative incidence of prostate cancer-specific mortality (PCSM) for men with intermediate to high-risk prostate cancer, by race (N = 116,084: White 84.0%, AA 16%; Gray's k-mean $P < 0.001$). *Previously published. [33]*

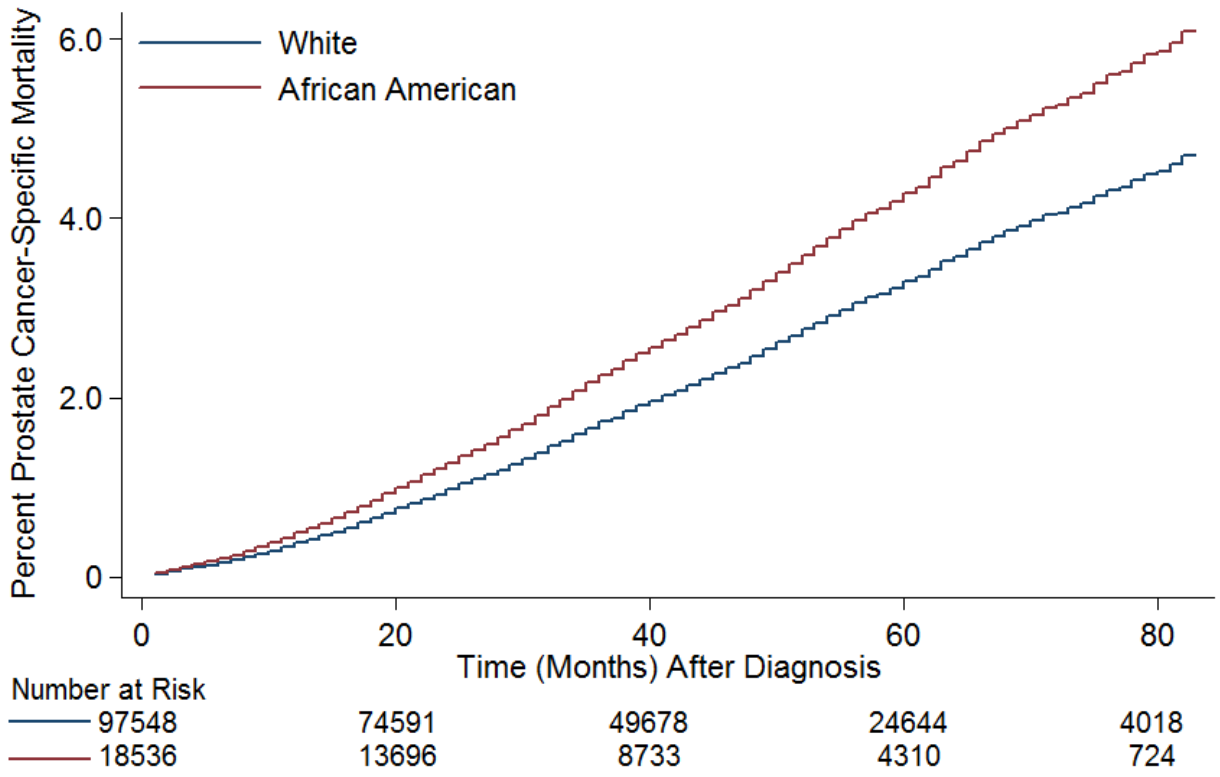

Figure 2. Plot of adjusted odds ratios and 95% confidence intervals along with trend line for the association between race (African American versus White [Referent]) and receipt of curative-intent treatment for men with high-risk prostate cancer (PSA > 20 or Gleason 8 – 10 or T3a – T4). Odds ratios are adjusted for age, marital status, income, education, residence, cancer stage, Gleason score, and PSA. ($P_{interaction}$ 2010 vs. 2004 = 0.490). *Previously published. [33]*

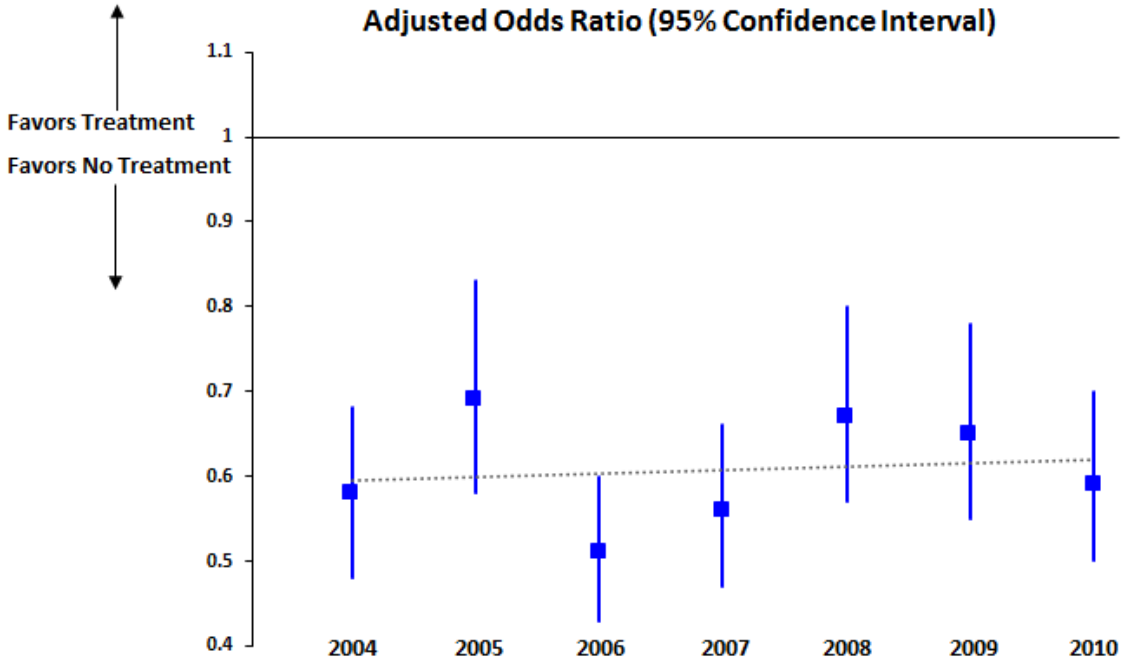

Figure 3. Adjusted odds ratios and associated 95% confidence intervals for the receipt of definitive treatment after adjusting for sociodemographics and cancer-specific prognostic factors, using white insured patients as the referent group (AOR 1.0). Abbreviations: AOR = Adjusted Odds Ratio; AA = African American. *Previously published. [38]*